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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,784	01/17/2002	Anita Mehta	RLL-192CIPUS	2737
26815	7590	07/14/2004	EXAMINER	
RANBAXY INC. 600 COLLEGE ROAD EAST SUITE 2100 PRINCETON, NJ 08540			MCKENZIE, THOMAS C	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/051,784	Applicant(s) MEHTA ET AL.	
	Examiner Thomas McKenzie, Ph.D.	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 April 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 16-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 27 is/are allowed.
- 6) ☒ Claim(s) 16-26 28-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This action is in response to amendments filed on 4/12/04. Applicant has amended claims 25-27, 31, 32, and 34. Applicant has canceled claim 39. Claims 16-26 and 28-38 were previously rejected. Claim 27 was designated as containing allowable subject matter. There are twenty-five claims pending and twenty-five under consideration. Claims 25-27 are compound claims. Claims 28 and 29 are composition claims. Claim 30 is a method of using claim. Claims 16-24 and 31-38 are method of making claims. This is the first action on the merits. The application concerns some piperazine linked oxazolidinone compounds, compositions, and uses thereof.

Response to Amendment

2. Applicants' amendments overcome the objections made in points #2-#5 of the previous office action. Applicants amendments overcome the indefiniteness rejections made in points #7, #9, #11-#13, and #16-#18. Applicants' amendments concerning the garbled provisos overcome the indefiniteness rejections made in points #8 and #10 of the previous action, but please see the new matter rejections made below in points #9 and #10 of this action.

Applicants' addition of hydrogen as a possible value for radical R in claims 25 and 31 broadens the claims and does not have literal support in the specification. However, Example 7, page 31 is an unsubstituted thiophene

compound with R = hydrogen. Applicants' addition of -CHO has to the list of R₁₂ variables has support in line 13, page 22 of the specification. Applicants' amendment that P and Q can be hydrogen does not have literal support in the specification but the working examples with furaldehyde and furanoic acid provide the implicit support for this expansion of the claim. Applicants' amendment that G = NH does not have literal support in the specification but does have implicit support in the working examples, which employ 1-substituted piperazine compounds. Applicants' limitation of their process claims to Pd(PH₃)₂Cl₂ as catalyst and W = CH₂, C(O), -C(O)-C(O)-, and CH₂(CO) overcome the enablement rejections made in points #19 and #20. Applicants' new proviso overcomes the art rejection over Pac (Bioorg.) made in point #21 but please see the new matter rejection made below.

3. Applicants' comments about claim 39 are noted. Claim 39 was rejected as indefinite in points #10, #12, and #18 and rejected as not enabled in point #20 of the previous office action. It was mistakenly not listed on the PTO-326 form or in the introduction of point #1 of the previous action. The Examiner regrets the error.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "a leaving group selected from *** -CHO" in claims 31 and 34 is used by the claim to mean "reactive group", while the accepted meaning of leaving group is "an atom or group (charged or uncharged) that becomes detached from an atom in what is considered to be the residual or main part of the substrate in a specified reaction.." Applicants addition of -CHO to the definition of R₁₂ has support in line 13, page 22 of the specification. However, the process B, in which -CHO is involved, is a reductive process. The -CHO does not become detached from the substrate furan ring but rather is converted into a CH₂ group. The term is indefinite because the specification does not clearly redefine the term leaving group. The Examiner suggests deleting "a leaving group" from the claims.

5. Claim 36 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 36 recites the limitation "Formula VI is furaldehyde" in line 2. This requires $M = \text{oxygen}$. There is no antecedent basis for these limitations in claim 34. Claim 34 appears to limit M to be sulfur.

Applicants argue that that variables P , Q , and R_{12} are now defined in independent claim 34. Yes, but M has also been defined to be sulfur and claim 34 requires it to be oxygen. The rejection is maintained.

6. Claim 37 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 37 recites the limitation "Formula VI is furoic acid" in line 2. This requires $R_{12} = \text{CO}_2\text{H}$, and $M = \text{oxygen}$. There is no antecedent basis for these two limitations in claim 34. There are three issues. Firstly, R_{12} cannot be CO_2H . Secondly, claim 34 does not define M to be oxygen.

Applicants argue that that variables P and Q are now defined in independent claim 34. Yes, but M has also been defined to be sulfur and claim 34 requires it to be oxygen. $R_{12} = \text{CO}_2\text{H}$ is not in the definitions in claim 34. The rejection is maintained.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The proviso in the last three lines of claims 25 and 31 lacks description. Nowhere in the specification is such a relationship linking the description among radicals R₁ U, V, W, T, and R described. Such a negative limitation requires description. In *Ex parte Grasselli, et al.* 231 USPQ 393, decided June 30, 1983, the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences said: "we agree with the examiner's position of record that the negative limitations recited in the present claims, which did not appear in the specification as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112." "It might be added that the express exclusion of certain elements implies the permissible inclusion of all other elements not so expressly excluded. This clearly illustrates that such negative limitations do, in fact, introduce new concepts."

8. The new proviso in the last three lines of claim 33 is rejected for the same reason.

9. Claims 26, 28-30, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to convey reasonably to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The new proviso in the definition of W has no support in the specification. In the previous office action, the Examiner asked if the phrase "heteroaryl except M = S, Q = P = H, W = (CO)" means when M = S, then Q = P = H and W = (CO), or when M = S and Q = P = H, then W = (CO), or must M always = S, Q = P always = H, and W always = (CO)? Applicants have chosen yet a different meaning. Applicants' new proviso that Q and P cannot be hydrogen is contrary to the plain meaning of "then Q = P = H". No skilled organic chemist would understand the previously garbled proviso to mean what Applicants now state.

Applicants argue their "intention in claim 26 was to exclude unsubstituted thiophene compounds when W is CO (carbonyl)" and "that the claim is not unclear". The Examiner agrees that the claim is no longer unclear. However, their intent in the application, as filed, was open to many different interpretations. The present interpretation by Applicants, in fact, is not one of the three of which the Examiner in the previous office action guessed. No skilled organic chemist would

understand the previously garbled proviso must mean only what Applicants now state.

10. Claims 34, 35, and 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The new proviso in the definition of R_{10} has no support in the specification. In the previous office action, the Examiner asked if the phrase "heteroaryl except $W = (CO)$, Q and $P = H$ and $M = S$, wherein $M = \text{Sulphur}$ " means mean when $W = (CO)$, then $M = S$ and $Q = P = H$, or does it mean when $Q = P = H$ and $W = (CO)$, then $M = S$? Or must M always = S , $Q = P$ always = H , and W always = (CO) or are only formula III being claimed or is Formula II claimed as well? Can M ever be NH or $N-CH_3$? Must it always be sulfur? Applicants have chosen yet a different meaning. Applicants' new proviso that Q and P cannot be hydrogen is contrary to the plain meaning of "then $Q = P = H$ ". No skilled organic chemist would understand the previously garbled proviso to mean what Applicants now state.

Applicants argue "that the intention in claim 34 was to exclude unsubstituted thiophene compounds when W is CO (carbonyl)" and "that the claim is not

unclear". The Examiner agrees that the claim is no longer unclear. However, their intent in the application, as filed, was open to many different interpretations. The present interpretation by Applicants, in fact, is not one of the three of which the Examiner in the previous office action guessed. No skilled organic chemist would understand the previously garbled proviso must mean only what Applicants now state.

Claim Rejections - 35 USC § 103

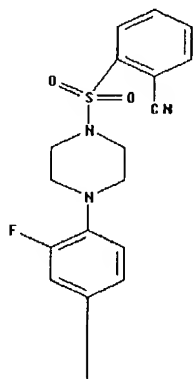
11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

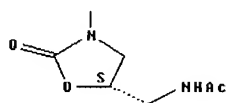
Claims 25 and 31 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Gadwood ('985). The reference teaches the compound with registry number 189038-61-7 shown below. The Applicant claims the compounds I with $R = \text{CN}$, $T = \text{benzene}$, $W = \text{S}$, $U = \text{hydrogen}$, $V = \text{fluorine}$, and $R_1 = \text{NHC(O)CH}_3$, with $R_2 = \text{methyl}$. The reference teaches a compound with $W = \text{SO}_2$. The compound is shown in the reference in lines 40-48, column 13. Compositions and treatment of microbial infections is taught in lines 16-26, column 16. The difference between the claimed and taught compounds is the oxidation state of the sulfur linker W. Applicants claim the reduced sulfide linker S and the reference teaches the oxidized sulfone linker SO_2 . Sulfides are commonly metabolized to sulfones *in*

vivo. It would be obvious to the skilled medicinal chemist, in view of the occurrence of cytochrome P450 and flavin-containing monooxygenase enzymes in the human liver to prepare such an oxidized metabolite from Applicants' compound. This would be expected to be a more stable active metabolite. The synthesis of the taught compound from the sulfonyl chloride makes obvious Applicants claim 31, which requires synthesis from a compound R-T-W-R₁₂. The leaving group R₁₂ taught in the prior art is chloride.

PAGE 1-A



PAGE 2-A



Applicants argue that there is no teaching in the reference that the taught sulfoxide can be formed *in vivo* by metabolic oxidation and no motivation presented to perform the required oxidation. This is not persuasive for two reasons. Firstly, if Gadwood ('985) taught the change in oxidation state, then the rejection would be anticipation (or at most inherency) not the present obviousness.

Secondly, the medicinal chemist of average skill in the art possesses the knowledge of in vivo sulfur oxidation and the motivation to apply that knowledge. Evidence of the knowledge level of the average artisan is provided by the graduate level textbook Foye (Principles of Medicinal Chemistry, 4ed) and the reference book Testa (Burger's Medicinal Chemistry, 5ed, Part I). Foye (Principles of Medicinal Chemistry, 4ed) states in the first complete paragraph, column 2, page 83 that "a greater knowledge of drug metabolism is becoming essential". Table 8-14, page 112 shows the oxidation of Applicants' claimed sulfides to the sulfone of the prior art. Testa (Burger's Medicinal Chemistry, 5ed, Part I) says in the first paragraph, page 130 "medicinal chemists engaged in drug discovery must be able to integrate metabolic considerations into drug design". The oxidation of Applicants claimed sulfide to the sulfone of the prior art is shown in reaction (2), page 144. These two references are not supplied to teach any deficiencies in Gadwood ('985), but rather to demonstrate the skill, knowledge, and motivation possessed in the medicinal chemistry arts.

Double Patenting

12. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101, which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention", in this context, means an

invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970). A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 16-24 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-9 of prior U.S. Patent No. 6,743,307. This is a double patenting rejection.

Applicants state they wish to await the allowance of the conflicting application. That conflicting application has now matured into a patent.

Allowable Subject Matter

13. Claim 27 is allowed. Claims 36 and 37 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

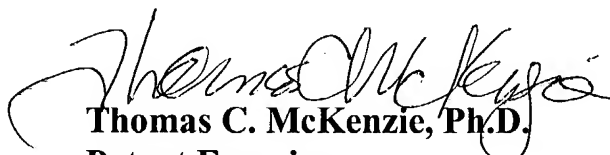
Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.**

See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

16. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact James O. Wilson, acting SPE of Art Unit 1624, at (571)-272-0661.


Thomas C. McKenzie, Ph.D.
Patent Examiner
Art Unit 1624

TCMcK/me